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| EXAMINER | |
|---|---|
| HAMA, JOANNE | |

| ART UNIT | PAPER NUMBER |
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| 1632 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/560,501 | MOOTHA ET AL. | |
| | Examiner | Art Unit | |
| | JOANNE HAMA | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,6,11-15,17,19,20,35,42,47,78,93 and 106-117* is/are pending in the application.

4a) Of the above claim(s) *1-3,6,11-15,17,19,20,35,42,47,78 and 113-117* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *93 and 106-112* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant filed an amendment to the claims March 6, 2008. Claims 4, 5, 7-10, 16, 18, 21-34, 36-41, 43-46, 48-77, 79-92, 94-105 are cancelled. Claims 106-117 are new. Claims 1-3, 6, 11-15, 17, 19, 20, 35, 42, 47, 78, 93, 106-117 are pending.

### *Election/Restrictions*

Applicant's election without traverse of Group 7 in the reply filed on March 6, 2008 is acknowledged.

Claims 1-3, 6, 11-15, 17, 19, 20, 35, 42, 47, 78 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 6, 2008. It is noted that Applicant has indicated that the further restriction of Groups 1-3 is traversed; however, Applicant indicates that none of Groups 1-3 was elected and Applicant will not present further detailed arguments with regard to this traversal (Applicant's response, page 9).

It is also noted that the Examiner has also withdrawn claims 113-117. Claims 113-117 have been withdrawn because they are drawn to methods distinct from that of the elected invention, a method of screening. Claims 113-114 require that the agent identified from the screen be assessed to have a particular activity. This method is not commensurate in scope with claim 93. Claims 115-117 are drawn to a method of treating of a mammal with a disease. A method of assessing whether an agent has a biological activity and a method of treating are restrictable from a method of screening

for an agent because the method steps used to characterize and treat are different and distinct from method steps used to screen for an agent. In addition to this issue, with regard to claims 115-117, it is noted that claim 93 is readable on in vitro and in vivo cells in which the method of screening is carried out. Since claim 93 encompasses in vivo screening, it is unclear why the agent would need to be administered again to a mammalian organism, per claims 115-117.

Claims 93, 106-112, drawn to a method of identifying an agent that regulates expression of OX-PHOS-CR genes, are under consideration.

### *Information Disclosure Statement*

Applicant filed an Information Disclosure Statement (IDS) on June 5, 2006. The IDS has been considered.

### *Specification*

The disclosure is objected to because of the following informalities: the figures do not match their legends. The legend for figure 3 (page 6 of the specification) indicates that there are figures 3a and 3b, but there is only one figure for figure 3. The legend for figure 4 indicates figures 4a-e. There are no "a-e" letters on the figure itself. Similarly, Figure 5 refers to 5a and 5a; there is no “a” or “b” for figure 5.

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 93, 106-112 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or

unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instant claims are drawn to a method of identifying an agent that regulates expression of OXPHOS-CR genes. The specification teaches the instant invention is to a method of identifying agents that treat a disorder characterized by reduced mitochondrial function, including that of impaired glucose tolerance and the diseases listed on page 21 of the specification (see also, specification, page 1, 2nd parag. under "Summary of the Invention", and page 4, 1st parag.). The specification teaches that OXPHOS-CR genes were identified in a microarray screen (specification, Example 3) and that the genes are a co-regulated subset of OXPHOS genes and which are strongly expressed in 3 of 46 tissues: skeletal muscle, heart, and brown fat. These tissues are major sites of insulin-mediated glucose disposal in mice (specification, Example 4). The specification also teaches that OXPHOS-CR genes are downregulated in tissues from diabetes mellitus 2 patients (DM2) and impaired glucose tolerance (IGT) patients, as compared to normal patients (specification, Example 4). While the specification indicates that OXPHOS-CR genes are downregulated in DM2 and IGT patients, the specification and art provide no guidance that any of the OXPHOS-CR genes are related to diabetes or mitochondrial diseases or disorders such that changing their expression pattern can be used to treat diabetes or a mitochondrial disease or disorder. That is, as far as can be told, decreased OXPHOS-CR gene expression taught by the specification appears to be correlative rather than causative of any disease or disorder. According to Smith, 2004, Nature, 428: 225-233, gene chips (which are a type of

microarray) measure correlative rather than causative events and it is difficult to sort out the "good" targets that have causative effects in diseases (Smith, page 229, 3rd col., 1st parag.). As such, because neither the specification nor the art provide any guidance of any relationship between OXPHOS-CR genes and diabetes or any mitochondrial disease or disorder, it would be undue experimentation for an artisan to use the agents identified in the claimed screen for treating diabetes or any mitochondrial disease or disorder.

In addition to this issue, the claimed method will identify agents that upregulate gene expression of at least two OXPHOS-CR genes, wherein the agents will treat diabetes or a mitochondrial disease or disorder. However, diseases such as diabetes are caused by many different genes and various environmental factors and it is unclear which pair of OXPHOS-CR genes would be used in the claimed screen to treat diabetes. As such, it would be undue experimentation for an artisan to practice the claimed invention without knowing which combination of OXPHOS-CR genes to use to treat diabetes or any other disease envisioned on page 20 of the specification.

In addition to this issue, the claims broadly encompass that the screening method be practiced in any animal. At the time of filing, Hoshikawa et al., 2003, Physiol. Genomics, 12: 209-219 teach that different animals have varying responses to disease and environmental stimuli. In their study, Hoshikawa et al. teach that mice and rats react differently to hypoxia, as evidenced by microarray gene anaylsis (Hoshikawa et al., abstract). As such, while the specification indicates that OXPHOS-CR genes are downregulated in diabetic human patients, the specification does not teach that

OXPHOS-CR genes are downregulated in other animal species such that upregulation of OXPHOS-CR genes in diseased animals will result in treatment of these animals for diabetes or increased mitochondrial activity. As such, while the specification teaches that the genes were identified in human, the specification does not provide guidance that other animals can be treated with agents obtained from the claimed screen using human OXPHOS-CR genes.

In addition to this issue, claim 93 encompasses identifying agents that decrease expression of OXPHOS-CR genes. According to the specification, OXPHOS-CR genes' expression levels are reduced in diabetic patients and in patients with reduced mitochondrial function. It is unclear how identifying a drug that further reduces OXPHOS-CR gene expression would treat diabetes or reduced mitochondrial function. Further, neither the art nor the specification indicates which of the diseases listed on page 20 of the specification would be treated by further decreasing OXPHOS-CR gene expression.

Thus, the claims are rejected.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 93, 106, 107 are rejected under 35 U.S.C. 102(b) as being anticipated by Burke et al., 1997, The Journal of Biological Chemistry, 272: 14705-14712.

Burke et al. teach that when yeast is put in an anaerobic condition, Cox5b mRNA increases in anaerobic conditions and Cyc1 mRNA decreases in anaerobic conditions (Burke et al., page 14707, Table 3). It is noted that lack of oxygen is interpreted as being the agent that regulates two OXPHOS-CR genes.

It is noted that claims 106, 107 are rejected because the claims are drawn to "potential" activities that the agent would have. As far as can be told, anoxia could potentially have these activities.

Thus, the claims are rejected.

## ***Conclusion***

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Joanne Hama/
Art Unit 1632